IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Patent Application No. 10/579,988

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Applicant: Leonard et al.

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DECLARATION UNDER 37 C.F.R. § 1.132 OF WARREN J. LEONARD, M.D.

I, Warren J. Leonard, M.D., do hereby declare:

1. I am a co-inventor of the subject matter disclosed and claimed in the above-captioned patent application (referred to herein as "the present invention"), which claims priority to U.S. Provisional Patent Application 60/523,754, filed on November 19, 2003. I am aware of the general knowledge available in the art and of the skill level of the ordinary artisan as it exists today and as it existed at the time U.S. Provisional Patent Application 60/523,754 was filed.

2. I have reviewed the Office Action from the U.S. Patent and Trademark Office (USPTO) dated January 4, 2010 regarding the present invention. I understand that the USPTO has rejected the pending claims of the present invention because the Office believes that the subject matter of the pending claims is obvious in view of the teachings of the Novak reference (U.S. Patent Application Publication 2003/0125524) and the Newell reference (U.S. Patent Application Publication 2003/0138433).

3. The pending claims of the present invention are directed to a method for enhancing an immune response in a subject and a method for treating a subject with a condition comprising a specific deficiency of at least one of memory B cells and plasma cells. The methods comprise (a) isolating a population of cells

comprising one or more of a mature B cell and a B cell progenitor from the subject; (b) contacting the population of cells comprising one or more of a mature B cell and a B cell progenitor with a composition comprising (i) an IL-21 polypeptide comprising the amino acid sequence of SEQ ID NO: 1 or (ii) a variant of the amino acid sequence of SEQ ID NO: 1, wherein the variant comprises the amino acid sequence of SEQ ID NO: 1 except for 1-5 amino acid substitutions, deletions, or additions, and wherein the variant retains the ability to bind to the IL-21 receptor and produce a physiological effect produced by binding of the IL-21 polypeptide comprising the amino acid sequence of SEQ ID NO: 1 to the IL-21 receptor, wherein the population of cells optionally is contacted with at least one antigen, and wherein the composition induces differentiation of at least one of the mature B cell and the B cell progenitor into one or more of a memory B cell and a plasma cell; (c) isolating or purifying one or more of the memory B cell and the plasma cell; and (d) introducing at least one of the memory B cell and the plasma cell into the subject, thereby enhancing the immune response.

4. I and my fellow co-inventors discovered that contacting a population of cells comprising one or more of a mature B cell and a B cell progenitor with a composition comprising IL-21 induces differentiation of the mature B cell and/or B cell progenitor into one or more of a memory B cell and a plasma cell. In particular, we discovered that IL-21 induces differentiation of human B cells into plasma cells and memory B cells.

5. In my opinion, prior to our discovery, an ordinary artisan would not have recognized that contacting an isolated population of mature B cells and/or B cell progenitors with IL-21 would induce differentiation of human B cells into plasma cells and memory B cells.

6. The Novak reference discloses the characterization of zalpha11 ligand, which is also known as IL-21.

7. The Novak reference generally mentions that "[p]roteins of the present invention are useful for stimulating proliferation, activation, differentiation and/or induction or inhibition of specialized cell function of cells of the involved homeostasis of the hematopoiesis and immune function," wherein hematopoietic lineages include, but are not limited to, T cells, B cells, NK cells, dendritic cells, monocytes, macrophages, and epithelial cells (see paragraph [0125] of the Novak

reference). However, the Novak reference does not correlate stimulation of proliferation, activation, differentiation and/or induction or inhibition with the particular cell types. In other words, the Novak reference lists various functions (i.e., stimulating proliferation, activation, differentiation, induction, and inhibition) and various cell types (T cells, B cells, NK cells, dendritic cells, monocytes, machrophages, and epithelial cells), but does not describe the relationship between the particular function and the particular cell type.

8. The Novak reference teaches that zalpha11 ligand (IL-21) stimulates the proliferation of B cells (i.e., increases the population of undifferentiated B cells) in response to activating stimuli (see Example 44 of the Novak reference). However, the Novak reference does not provide any specific teaching or evidence that contacting IL-21 with a population of mature B cells and/or B cell progenitors results in the differentiation of the mature B cells and/or B cell progenitors into memory B cells and/or plasma cells.

9. The Newell reference merely discloses that a primary encounter with an antigen can stimulate specific B cells to differentiate into cells that produce antibody at a high rate (plasma cells) and populations of memory cells (see paragraph [0010] of the Newell reference). The Newell reference does not disclose IL-21, let alone that contacting IL-21 with a population of mature B cells and/or B cell progenitors results in the differentiation of the mature B cells and/or B cell progenitors into memory B cells and/or plasma cells.

10. I hereby declare that all statements made herein of my own knowledge are true, that all statements made on information and belief are believed to be true, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Date: 4/27/2010

Warren J. Leonard, M.D.